Anorectal and Enteric Infections in Homosexual Men

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Homosexual men are at increased risk for traditional sexually transmitted anorectal infections (gonorrhea, syphilis, venereal warts, herpes and chlamydial infection) and enteric infections characterized by a low infecting inoculum (hepatitis A and B, amebiasis, giardiasis, shigellosis and campylobacteriosis). Infections account for most of the gastrointestinal symptoms in homosexual men seen at sexually transmitted disease clinics, but asymptomatic and polymicrobial infections are also common. Distinguishing three syndromes—proctitis, proctocolitis and enteritis—is clinically useful because these syndromes correlate with specific microorganisms and modes of transmission. A careful anoscopic examination, rectal Gram's stain, cultures for gonorrhea and chlamydia, VDRL and darkfield examination of suspicious lesions should be routinely done when sexually active homosexual men present with unexplained gastrointestinal symptoms. Based on the history, physical examination and initial laboratory studies, patients can usually be classified as having proctitis, proctocolitis or enteritis. This distinction facilitates selection of both confirmatory diagnostic tests and antimicrobial therapy. The effectiveness of empiric treatment regimens for asymptomatic sexual contacts or for symptomatic patients in whom microbiological tests are pending has not been studied.

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Homosexual men have a high incidence not only of anorectal gonorrhea, syphilis, venereal warts and herpes infection[1,2] but also of several enteric infections not traditionally considered sexually transmitted—hepatitis A[3] and B,[4] amebiasis,[5] giardiasis,[6] shigellosis[7] and campylobacteriosis.[8] While these sexually transmitted enteric infections can usually be diagnosed and treated if they are suspected, physicians must be aware of patients' sexual preference and practices, must be attuned to the etiology and spectrum of anorectal and intestinal infections in homosexuals and must have an approach to diagnosis and treatment and to counseling of infected homosexual patients. In this article we will review common sexually transmitted gastrointestinal infections in homosexual men and discuss their diagnosis and management.

Risk Factors

The high risk of acquiring sexually transmitted diseases (STD) for homosexual men arises from several factors, including multiple sexual partners, anonymous partners, frequent asymptomatic infections and specific sexual practices such as rectal intercourse and direct or indirect oral-anal contact.[9] Additionally, many clinics and physicians have limited access to diagnostic laboratory tests for some of these infections, leading to nonspecific treatment, inability to recognize asymptomatic infections and little or no treatment of sexual partners. The combined effects of all these factors make it very difficult to interrupt disease transmission. Knowledge of these risk factors, however, recognition of the clinical syndromes produced by these infections and proper treatment and counseling will help decrease the risk of acquiring and transmitting STD among homosexual men.

Clinical Syndromes

A clinically useful approach to determining the cause of gastrointestinal symptoms in gay men involves classifying patients' presenting complaints into three syndromes—proctitis, proctocolitis and enteritis.[10] Symptoms associated with

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ABBREVIATIONS USED IN TEXT

LGV = lymphogranuloma venereum
PPNG = penicillinase-producing *Neisseria gonorrhoeae*
RPR = rapid plasma reagin
STD = sexually transmitted diseases

proctitis include anorectal pain, mucopurulent or bloody rectal discharge, tenesmus and constipation. Symptoms of enteritis include diarrhea, abdominal pain, bloating, cramping and the absence of anorectal symptoms. Proctocolitis produces overlapping symptoms of both proctitis and enteritis.

Anoscopic or sigmoidoscopic examination helps to classify patients into these three diagnostic categories. Patients with proctitis and proctocolitis usually have rectal exudates or rectal bleeding (or both) on anoscopy. If sigmoidoscopy is done, patients with proctitis have disease limited to the rectum, whereas patients with proctocolitis have disease extending at least into the sigmoid colon. Patients with enteritis usually have normal findings on anoscopy and sigmoidoscopy, but have inflammation of the small intestine or more proximal colon (Table 1).

By classifying patients based on their presenting symptoms and signs into these three syndromes, Quinn, Stamm and co-workers[10] were able to associate each syndrome with certain sexually transmitted diseases. They studied 119 homosexual men presenting to an STD clinic with intestinal symptoms and 75 asymptomatic homosexual men presenting for screening at the same clinic. At least 80% of the symptomatic and 40% of the asymptomatic patients were infected with sexually transmissible enteric or rectal pathogens. *Neisseria gonorrhoeae,* herpes simplex virus, non-lymphogranuloma venereum (LGV) strains of *Chlamydia trachomatis* and *Treponema pallidum* were each associated with signs and symptoms of proctitis (Table 1). *Campylobacter jejuni, Shigella flexneri,* LGV strains of *C trachomatis, Entamoeba histolytica* and *Clostridium difficile* produced the symptoms and signs of proctocolitis. *Giardia lamblia* was associated with enteritis. Of the symptomatic patients, 22% had two or more pathogens detected but only 4% of the asymptomatic men had multiple infections. In this study, abnormal findings on anoscopy or the presence of increased numbers of polymorphonuclear leukocytes on rectal Gram's stain, or both, correlated with proctitis and proctocolitis, even in asymptomatic patients. In dealing with homosexual patients, therefore, physicians must consider not only the presenting spectrum of symptoms and signs produced by individual pathogens, but also the possibility of a polymicrobial infection. The high prevalence of asymptomatic infections in this population also deserves emphasis.

Proctitis and Proctocolitis Caused by Anorectal Pathogens

Neisseria gonorrhoeae

N gonorrhoeae is perhaps the most common STD pathogen seen in gay men.[2] Infection usually occurs by direct inoculation of *N gonorrhoeae* into the rectal mucosa during anal intercourse with an infected partner. Anorectal gonorrhea may be symptomatic or asymptomatic. If symptoms are present, they usually consist of mild anorectal pain, itching and mucopurulent discharge. In some cases, more impressive tenesmus and secondary constipation occur.[10] On anoscopy, findings are usually limited to mucopus in the anal canal, especially in the anal crypts. A rectal Gram's stain aids in the diagnosis if positive, but its sensitivity is only 30% to 40% compared with culture, the confirmatory diagnostic test. Homosexual men with uncomplicated anorectal gonococcal infection should receive aqueous procaine penicillin G, 4.8 million units, plus 1 gram of probenecid. For penicillin-allergic patients, administration of spectinomycin hydrochloride, 2 grams given intramuscularly, is the treatment of choice. All sexual contacts should be examined, cultures done and the person(s) treated, and the patient should be counseled to abstain from sex until he has had a negative culture showing cure. A test-of-cure culture should be done five to ten days after treatment.

Penicillinase-producing *N gonorrhoeae* (PPNG) has been identified in the United States since 1976. PPNG infections do occur in homosexual men, but sustained transmission among them has been infrequent.[11] Because rates vary considerably by locale, physicians should be aware of the prevalence of PPNG in their own communities. The current recommended treatment of uncomplicated cases of anogenital PPNG infection is spectinomycin, 2 grams given intramuscularly, or cefoxitin, 2 grams in a single intramuscular dose, given with probenecid, 1 gram by mouth. Pharyngeal infection can be treated with trimethoprim-sulfamethoxazole (80/400 mg), nine tablets by mouth every day for five days. Test-of-cure cultures and contact tracing and treatment of partners are extremely important to limit transmission of PPNG strains.

TABLE 1.—*Syndromic Classification of Gastrointestinal Infections in Homosexual Men*

Characteristics	Syndromes		
	Proctitis	Proctocolitis	Enteritis
Pathogen	*Neisseria gonorrhoeae,* herpes simplex virus, *Chlamydia trachomatis, Treponema pallidum*	*Entamoeba histolytica, Campylobacter jejuni, Shigella, Chlamydia trachomatis,* (LGV type)	*Giardia lamblia*
Mode of transmission	Receptive anal intercourse	Direct or indirect fecal-oral contact	Direct or indirect fecal-oral contact
Symptoms	Anorectal pain, burning, discharge, tenesmus	Symptoms of proctitis plus enteritis, hematochezia	Diarrhea, abdominal pain, cramps, nausea, bloating
Anoscopic findings	Abnormal	Abnormal	Normal
Sigmoidoscopic findings	Normal above 15 cm	Abnormal above 15 cm	Normal

LGV = lymphogranuloma venereum

Chlamydia trachomatis

The spectrum of disease resulting from *C trachomatis* rectal infection ranges from the absence of symptoms to severe granulomatous proctitis, in part dependent on the serovar of the infecting *C trachomatis* strain.[12,13] Strains of the LGV serovars cause more severe disease, often an acute proctocolitis with bloody diarrhea, fever, a mucopurulent rectal discharge and severe tenesmus. Inguinal adenopathy is not as prominent with rectal LGV infections as with genital infections, but may be present. On anoscopy, ulcers may be seen. The findings on rectal biopsy specimens obtained from patients with LGV infection can histologically mimic idiopathic inflammatory bowel disease.[14] In LGV-strain infection, antichlamydial antibody titers as determined by the complement fixation test available in most state laboratories are typically greater than or equal to 1:64.

Infections with non-LGV strains of *C trachomatis* usually produce only mild anorectal symptoms or are asymptomatic. Like *N gonorrhoeae* infections, they usually involve the distal rectal mucosa and anal crypts and are acquired by direct rectal inoculation via anal intercourse with an infected partner. Diagnosis can be confirmed by culture for *C trachomatis*, or can be suspected when a rectal Gram's stain shows persistent polymorphonuclear leukocytes and cultures are negative for gonorrhea.

Infection with *C trachomatis* responds to treatment with tetracycline or doxycycline. A case of non-LGV infection can be treated with a regimen of tetracycline hydrochloride, 500 mg by mouth four times a day for one week, while cases of LGV infection should be treated at least two weeks on the same regimen. Residual strictures or fistulas may require surgical intervention. Alternate regimens for patients with tetracycline intolerance or fixed drug eruptions are listed in Table 2.

Herpes Simplex Virus

Most cases of herpetic proctitis are caused by herpes simplex virus type 2 and are acquired by direct inoculation via rectal intercourse.[15] Primary infection usually produces severe anorectal pain, fever, tenesmus, hematochezia and rectal discharge. Constitutional symptoms include fever, chills, malaise and headache, but rarely stiff neck, photophobia or meningeal signs. Urinary retention, S4-5 dysesthesias and impotence, however, occur in as many as 50% of cases of primary rectal herpes simplex virus infection and are unique clinical findings distinguishing herpes simplex infection from other forms of proctitis. Anoscopy or sigmoidoscopy usually shows intact vesicopustular lesions or shallow ulcers, and a biopsy specimen shows microulcerations, intranuclear inclusions or perivascular lymphocyte cuffing. The characteristic clinical features permit most cases to be diagnosed on clinical grounds alone, but the diagnosis can be confirmed by culture, preferably taken from the base of one or more freshly opened vesicular lesions.

There is no definitive treatment for herpes simplex virus proctitis, though studies are under way with various antiviral agents, including acyclovir. Supportive care, hydration, catheterization for urinary retention and admission to hospital for severe disease are recommended. In severe cases, a therapeutic trial of acyclovir given orally or intravenously may be warranted despite the absence of published information regarding its use. Little is known about the frequency or severity of recurring episodes.

Syphilis

Nearly half of the reported cases of early syphilis in the United States occur in homosexual men.[16] Anorectal chancres usually appear within two to six weeks after exposure by rectal intercourse. Primary anorectal syphilis can be asymptomatic and thus remain unrecognized by a patient or may be painful and misdiagnosed as traumatic lesions, fissures or hemorrhoids. In suspected cases, it is therefore of great importance to examine the perirectal area and anal canal via anoscopy for the lesions of primary syphilis, which may appear as a classic chancre or may mimic polyps, smooth lobulated masses or mucosal ulcerations. Condyloma lata, lesions of secondary syphilis, are also found near or within the anal canal and can easily be confused with anal warts. The lesions, however, are usually teeming with spirochetes, and thus a darkfield examination is positive.

Early syphilis can be diagnosed using anoscopy, darkfield examination of perianal lesions and serology. The VDRL or rapid plasma reagin (RPR) test may be negative in a case of early primary disease, but is positive in virtually all patients

TABLE 2.—*Treatment Regimens for Gastrointestinal Infections in Homosexual Men*

Pathogen	*Treatment Regimen*	*Alternative Regimen*
Neisseria gonorrhoeae	Procaine penicillin G, 4.8 million units given IM, + 1 gram probenecid PO	Spectinomycin hydrochloride, 2 grams IM
Chlamydia trachomatis	Tetracycline, 500 mg PO qid for 7 to 14 d	Erythromycin, 500 mg PO qid for 7 to 14 d
Herpes simplex virus	Supportive, or acyclovir, 400 mg PO qid for 7 d	
Early syphilis	Penicillin G benzathine, 2.4 million units IM	Tetracycline, 500 mg PO qid for 15 d Erythromycin, 500 mg PO qid for 15 d
Campylobacter species	Erythromycin, 500 mg PO qid for 7 d	Tetracycline, 500 mg PO qid for 7 d
Shigella species	Trimethoprim/sulfamethoxazole, 1 tablet (160/800 mg) PO bid for 7 d	Ampicillin, 500 mg PO qid for 7 d Tetracycline, 1.5 grams PO as a single dose
Entamoeba histolytica		
Symptomatic	Metronidazole, 750 mg PO for 5 to 10 d, + iodoquinol, 650 mg PO tid for 20 d	Metronidazole, 750 mg PO tid for 5 to 10 d, or Paromomycin sulfate, 25 to 30 mg/kg/d in 3 divided doses for 7 d
Asymptomatic	Iodoquinol, 650 mg PO tid for 20 d	Diloxanide furoate, 500 mg PO tid for 10 d
Giardia lamblia	Quinacrine hydrochloride, 100 mg PO tid for 7 d	Metronidazole, 250 mg PO tid for 7 d

IM=intramuscularly, PO=orally, qid=4 times a day, bid=twice a day, tid=3 times a day

with secondary syphilis. The fluorescent treponemal antibody-absorption test usually becomes positive before the VDRL, and may thus be useful in patients with suspected early syphilis. If a biopsy of suspicious lesions is done, the specimen should be processed for silver staining or for specific immunofluorescence to *T pallidum* as well as for routine histology.[17] A patient with early syphilis should be treated with penicillin G benzathine, 2.4 million units given intramuscularly at a single session. Penicillin-allergic patients should receive tetracycline hydrochloride, 500 mg by mouth four times a day for 15 days. All contacts should be examined, screened and treated.

Proctocolitis and Enteritis Due to Enteric Pathogens

In the past decade, *Shigella, Giardia, E histolytica, Salmonella* and *Campylobacter* have been identified as enteric pathogens in homosexual men. In some cities, sexually transmitted cases may account for a substantial proportion of all reported cases of certain of these infections. For example, from 30% to 50% of cases of *Shigella* reported to the health departments in New York, San Francisco and Seattle-King County occur in homosexual men.[7,18,19] Sexual activity involving direct or indirect fecal-oral contact is the apparent mode of transmission of these infections, most of which can be transmitted by as few as 10 to 100 organisms.

Shigella

Shigellosis in homosexual men often presents with the classic abrupt onset of nausea, cramping, fever and watery diarrhea containing mucus, blood or pus, but also can be asymptomatic.[7] Sigmoidoscopic examination shows mucosal inflammation and friability. Cultures of stool or rectal swabs on selective media (MacConkey's or Shigella and Salmonella agar) confirm the diagnosis. Treatment includes hydration and antibiotics, generally trimethoprim-sulfamethoxazole, 160/800 mg (double strength) taken orally twice a day for seven days. Ampicillin can also be given but many strains show in vitro resistance in some parts of the country. Although the value of treating sexual contacts of infected gay men is not known, it seems reasonable from a public health point of view to screen and treat partners.

Campylobacter Species

C jejuni has become the most common bacterial cause of acute diarrhea in many communities. *Campylobacter* infection is generally acquired by ingesting contaminated food or water, and sexual transmission among homosexual men by fecal-oral contact has not been as clearly shown as has transmission of *Shigella.*[18] However, recent studies have identified *C jejuni* in symptomatic and asymptomatic homosexual men in higher frequency than in matched groups of heterosexual men. A heterogeneous group of newly described *Campylobacter*-like organisms may also produce diarrhea in gay men.[10,20] Diarrhea, abdominal bloating, mucopurulent rectal discharge or mucus-coated stools have been the most common symptoms and signs in homosexual men with *C jejuni* infection. Anoscopic and sigmoidoscopic findings are similar to those described for shigellosis. Infection can be confirmed using selective culture systems that prevent overgrowth of other fecal flora and provide the necessary microaerophilic environment at 42°C, optimal for *C jejuni.*[21]

Patients with *Campylobacter* infections should be treated with a one-week course of erythromycin, 500 mg taken by mouth four times a day. Treatment may shorten the duration of symptoms and clearly decreases the period of fecal shedding. The management of sexual contacts has not been studied, but they should probably be screened and treated empirically.

Parasitic Infections in Homosexual Men

Giardiasis and amebiasis have become endemic in certain homosexual populations, largely because of the high prevalence of asymptomatic infection in these men combined with the frequent use of sexual practices that involve direct or indirect fecal-oral contact. In cases of *E histolytica* infection, symptoms may be absent or severe, including diarrhea, blood or mucus-coated stools, cramps, bloating and fever. Findings on sigmoidoscopy may be normal or include diffuse inflammation and ulceration of the distal colon. Microscopic identification of trophozoites or cysts in a direct stool smear confirms the diagnosis. Symptomatic patients should be treated with metronidazole hydrochloride, 750 mg given orally three times a day for five to ten days, plus iodoquinol, 650 mg by mouth three times a day for 20 days.[22] Alternative treatment regimens include metronidazole given alone or paromomycin sulfate, 25 to 30 mg per kg in three divided doses for seven days, followed by a luminal amebicide such as iodoquinol if clinical cure is not achieved. The importance of treating asymptomatic cyst passers or sexual partners of proven cases is still unclear, but seems reasonable from a public health point of view. In some studies, however, *E histolytica* strains isolated from asymptomatic homosexual men have been largely nonpathogenic by zymodeme typing, and thus further study of the clinical importance of such infections is needed.[23]

Giardia lamblia infection produces symptoms ranging from mild to severe, with abdominal cramps; bloating; frequent, greasy, loose stools; chronic diarrhea; anorexia, and weight loss. Findings at sigmoidoscopy are generally normal because the organism typically parasitizes the duodenum and jejunum. The diagnosis is confirmed by identifying cysts or trophozoites in direct examinations of stool smears or in duodenal aspirate or biopsy specimens if stool smears are negative. Treatment regimens include quinacrine HCl, 100 mg three times a day for five to seven days, or metronidazole, 250 mg by mouth three times a day for ten days. Sexual partners should be screened and treated.

Three stool specimens should optimally be collected to diagnose parasitic infections in homosexual men. These specimens should be collected two or more days apart and should be delivered to a laboratory within an hour of collection, or should be placed in polyvinyl alcohol and 10% formalin preservative. The patient should not be taking antibiotics, antidiarrheal agents containing bismuth or kaolin, magnesium hydroxide or mineral oil. Barium in the gut lumen also interferes with parasite identification, and thus contrast studies should be done after the patient has collected the stool specimens.

Enterobius vermicularis, Iodamoeba buetschlii and *Dientamoeba fragilis* have also been described as sexually transmitted pathogens in homosexual men, but occur infrequently.[24-26] Various nonpathogenic parasites may also

appear in the stool of homosexual men, including *Entamoeba coli, Entamoeba hartmanni, Endolimax nana* and *Chilomastix mesnili.* At this time, these agents are not considered pathogenic and their presence does not require treatment.

Approach to a Homosexual Patient With Possible Gastrointestinal Infection

Given the polymicrobial nature of sexually transmitted gastrointestinal infections in homosexual men and the similar clinical presentations produced by many of these pathogens, physicians must use a systematic diagnostic approach. Doing cultures and stool examinations for all potential pathogens in each patient is prohibitively expensive and can probably be avoided in most patients if one uses an approach like that outlined in Figure 1.[10]

As always, the history and physical examination provide important clues to the diagnosis. In dealing with homosexual patients, physicians must ask about specific sexual practices, as well as the number of recent sexual contacts, to evaluate the risk of infection. A careful genital examination, including inspection of the perirectal skin, the anus and the anal canal by anoscopy, is indispensable and may identify hidden chancres, ulcers or abscesses, as well as determining the extent and severity of infection.

Selected rapid diagnostic tests should be done during the initial examination. A rectal Gram's stain should be done in all homosexual patients with rectal symptoms and may show intracellular Gram-negative diplococci diagnostic of *N gonorrhoeae.* Even in the absence of gonococci, a Gram's stain that shows one or more polymorphonuclear leukocytes per oil immersion field should strengthen the physician's suspicion of an infectious cause for proctitis or proctocolitis symptoms. The initial laboratory evaluation should always include a VDRL, or an RPR test if the physician is particularly suspicious of syphilis. For all suspicious masses or ulcers, a dark-field examination should be done on fluid exudate. All homosexual patients should have rectal screening cultures for *N gonorrhoeae* and *C trachomatis* (if available) on initial examination. Herpes simplex virus infections can often be diagnosed clinically, but cultures from the base of vesicles or ulcers will provide a definite diagnosis.

Based on the history, physical examination and initial laboratory studies, a physician can usually classify a patient as having proctitis, proctocolitis or enteritis and can treat any pathogens identified in the diagnostic tests outlined above. In addition, stools for enteric-pathogen cultures and ova and parasite examination should be sent for patients with proctocolitis or enteritis. The effectiveness of empiric treatment

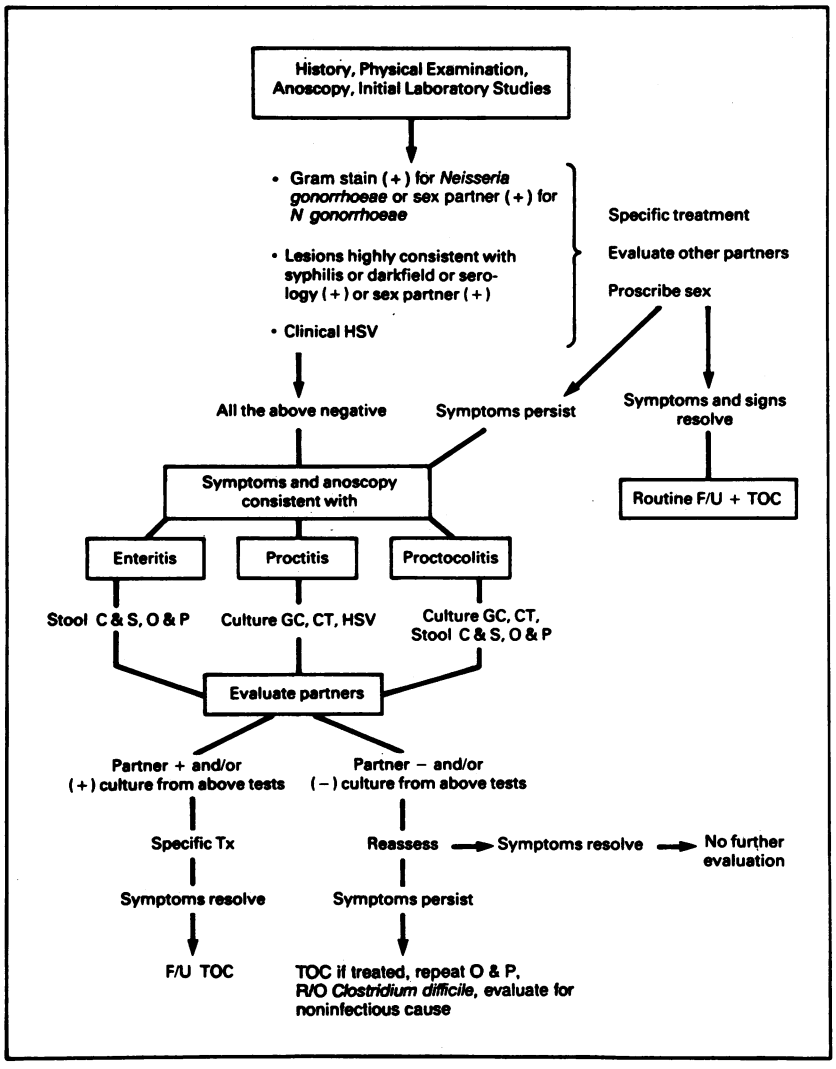

Figure 1.—Algorithm for managing anorectal or intestinal symptoms or both in homosexually active men (adapted from Quinn et al[10]). HSV = herpes simplex virus, F/U = follow-up, TOC = test of cure [culture], C & S = culture and sensitivity, O & P = ova and parasites, GC = gonococcus [smear], CT = *Chlamydia trachomatis,* Tx = treatment

TABLE 3.—*Possible Noninfectious Causes of Intestinal Symptoms in Homosexual Men*

Ulcerative colitis	Polyps
Crohn's disease	Ulcers
Hemorrhoids	Trauma
Fissures	Foreign bodies
Fistulas	Rectal carcinoma
Irritable bowel syndrome	Lactose intolerance

regimens given while microbiologic test results are pending has not been studied. If symptoms are mild, treatment should be deferred until results are available, and noninfectious causes should also be considered. Alternatively, in patients with more severe symptoms in whom the suspicion of an infectious cause is high, we have used empiric treatment regimens such as aqueous procaine penicillin, 4.8 million units given intramuscularly, plus 1 gram of probenecid given orally, followed by tetracycline, 500 mg by mouth four times a day for one week, for patients with proctitis or proctocolitis, and metronidazole, 250 mg by mouth four times a day for one week, for patients with enteritis symptoms. All patients should be reassessed for resolution of symptoms and signs, and should have test-of-cure evaluations for identified pathogens. Should symptoms persist after appropriate treatment for one infection, other pathogens should be sought. If no pathogens are identified and symptoms persist, the patient may require gastroenterologic workup for possible inflammatory bowel disease or other noninfectious processes (Table 3). Sexual partners should be evaluated and empirically treated for gonorrhea and syphilis if these infections were identified in the index case. For other infections, studies supporting the effectiveness of empiric therapy are lacking, and partners should be evaluated microbiologically and treated only for specific identified infections. Counseling regarding the symptoms of sexually transmitted enteric infection and their modes of transmission should be provided.

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